Current trends in European renal epidemiology

Heaf, James

Published in:
Clinical Kidney Journal

DOI:
10.1093/ckj/sfw150

Publication date:
2017

Document version
Publisher's PDF, also known as Version of record

Clinical Kidney Journal

ckj

OXFORD

Leading European Nephrology

Clinical Kidney Journal, 2017, vol. 10, no. 2, 149–153

doi: 10.1093/ckj/sfw150
Advance Access Publication Date: 18 February 2017
Editorial Comment

EDITORIAL COMMENT

Current trends in European renal epidemiology

James Heaf

Department of Medicine, Zealand University Hospital, Roskilde, Denmark

Correspondence and offprint requests to: James Heaf; E-mail: heaf@dadlnet.dk

Abstract

The incidence of end-stage renal disease (ESRD) continues to vary substantially between the countries in Europe that contribute data to the ERA-EDTA Registry. Differences can be attributed to socioeconomic factors and prophylaxis programs for patients with chronic kidney disease (CKD) and may also express real differences in CKD incidence. Recently, age-adjusted ESRD incidence has begun to fall in many countries, probably related to improved prophylaxis. However, absolute rates may increase, partly due to socioeconomic advances in countries with a low gross domestic product and partly due to continuing increases in the proportion of elderly patients. Prevalence rates are expected to continue to increase, mainly due to increases in relative transplant prevalence, improved graft survival times and continuing improvements in both dialysis and transplant patient survival. Overall treatment results continue to improve.

Key words: dialysis, epidemiology, Europe, transplantation

Introduction

This issue contains details from the ERA-EDTA Registry's annual report for 2014 [1]. The registry and its contributing national and regional registries are to be congratulated for this continuing work, particularly because the effort involved is to a large extent voluntary. It has documented the evolution of European renal end-stage renal disease (ESRD) epidemiology since 1964, primarily through the publication of annual reports [2–5] and reviews of epidemiological trends [6–11]. The first publication [12] described the treatment of 271 dialysis patients, but already by the 1971 report [13], details of 9411 dialysis and renal transplant patients from 24 countries were available, corresponding to a prevalence of 22 patients/million population (ppm)/year. Prevalence has continued to increase: 1980, 118; 1990, 224; 1999, 583 [14]; 2010, 741 [2] and now 924 ppm. Data are available from 35 countries. Seven countries are currently not contributing data, the most important being Germany and Russia. Because the number and identities of contributing countries changes over time, overall year-on-year comparisons should be treated with caution.

The end of the ESRD epidemic?

It has been some years since renal replacement therapy (RRT) incidence rates started to stabilize in Europe [8, 15, 16]. Developments in European epidemiology between 2001 and 2011 for countries supplying the ERA-EDTA Registry with individual data have recently been reviewed [10, 11]. The most remarkable finding was that, for the first time, incidence rates fell in most countries reporting individual data, with an overall age-adjusted decrease from 131 to 124 ppm between 2008 and 2011. However, the unadjusted rate for Europe as a whole has continued to increase slightly, from 124 ppm in 2010 [2] to 133 ppm in 2014, mainly due to a continuing increase in the average age at RRT initiation from 61.0 to 64.6 years. Thus previous fears of a continuing increase in incidence >140 ppm [17] have been allayed. In Finland,

Received: December 22, 2016. **Accepted:** December 22, 2016

the present rate of 81 ppm (previously 93) is among the lowest in Europe. In Denmark, the decrease has been most notable among the elderly with, for example, an approximate halving of the incidence since 2001 among 60–69 year olds, from 400 to 218 ppm [18], associated with a concurrent large increase in antihypertensive drug use, particularly drugs blocking the renin–angiotensin system (RAS) [19]. Although the number of transplanted patients in Denmark continues to increase, the number of dialysis patients has fallen by 9% since 2008. Other countries with notable decreases in incidence include Austria and Norway [10]. Similar changes have been noted in the USA, albeit from a higher base: adjusted incidence has fallen from 387 to 354 ppm, and for patients >74 years, from 1,801 to 1,556 ppm [20]. Somewhat surprisingly, considering the rising incidence of type 2 diabetes mellitus (DM) in Europe and the USA [21], incidence rates of RRT for diabetic nephropathy have stabilized in Europe at ∼32 ppm, and have actually fallen in the USA from 175 to 156 ppm. These findings suggest that a well-organized program for prophylactic treatment of chronic kidney disease (CKD) can reduce the incidence of RRT and ultimately prevalence. However, prevalence will generally continue to increase for some time to come, with the actual exception of Finland, where absolute prevalence is expected to remain stable [22]. There are several causes: there is a lag time between changes in incidence and subsequent changes in prevalence, some countries will continue to increase RRT acceptance rates due to social and economic progress and background population age will continue to increase, resulting in a greater difference between standardized and real incidence rates. Finally, RRT survival continues to increase.

Improved survival

Treatment results have improved throughout the history of modern nephrology; this trend continues for all treatment modalities and is substantial. Thus, compared with the 2001–2005 cohort [2], the 2008–2012 cohort shows a decrease in adjusted RRT mortality at 2 years from 21 to 16.2%, dialysis mortality from 24.0 to 18.9%, transplant mortality (dead donor) from 4.3 to 3.2%, transplant mortality (living donor) from 3.2 to 1.4%, graft loss (dead donor) from 12.1 to 9.8% and graft loss (living donor) from 8.8 to 5.4%, with the 2005–2009 cohort showing intermediate results. Renal transplant has probably benefitted from improved immunosuppressive therapy and preoperative and postoperative care. The improvement in dialysis mortality is more surprising considering the general paucity of therapeutic randomized trials with positive results [23–26], but may be due to a generally successful therapeutic response to epidemiological studies: better control of hyperphosphatemia, hypercalcemia and hyperparathyroidism [27]; vitamin D therapy [28]; blood pressure [29]; hydration [29, 30] and better predialysis preparation [31].

The report also shows a continuing adjusted survival advantage for peritoneal dialysis (PD) relative to hemodialysis (HD) for the first 4 years of therapy. This phenomenon has been described many times before [32] and is independent of preexisting comorbidity and predialysis planning [33]. The difference seems to be increasing [11, 33]. It may be causal; possible factors include better preservation of residual renal function [34], the continuous nature of PD [35] and reduced intradialytic side effects [36].

Differences in RRT incidence

One striking finding in the report is the large variation in incidence between countries, ranging from 23 ppm in Ukraine to 237 ppm in Portugal. Among the ERA-EDTA Registry's many initiatives, the EVEREST study [37] sought to identify factors determining the wide variation in RRT incidence throughout the world. Gross domestic product (GDP) per capita, percentage of GDP spent on health care, dialysis facility reimbursement rate and private for-profit share of HD facilities were all found to be important. Although there is little overall correlation between

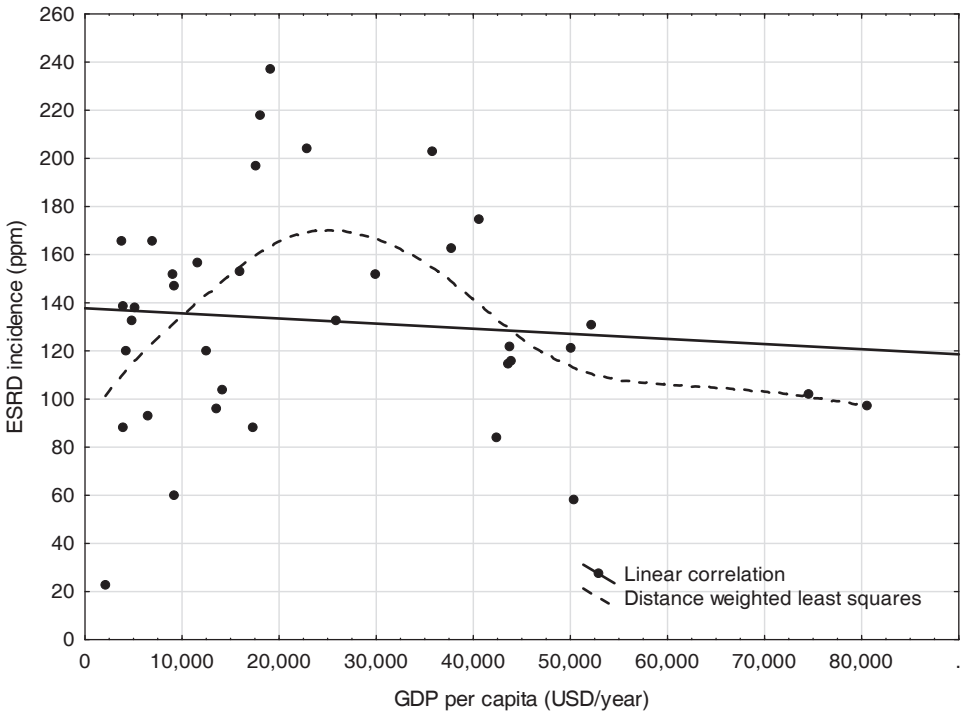

Fig. 1. Relationship of per capita GDP (International Monetary Fund 2015 figures) to RRT incidence in Europe in 2014. Incidence: unadjusted figures in patients/million population (ppm)/year.

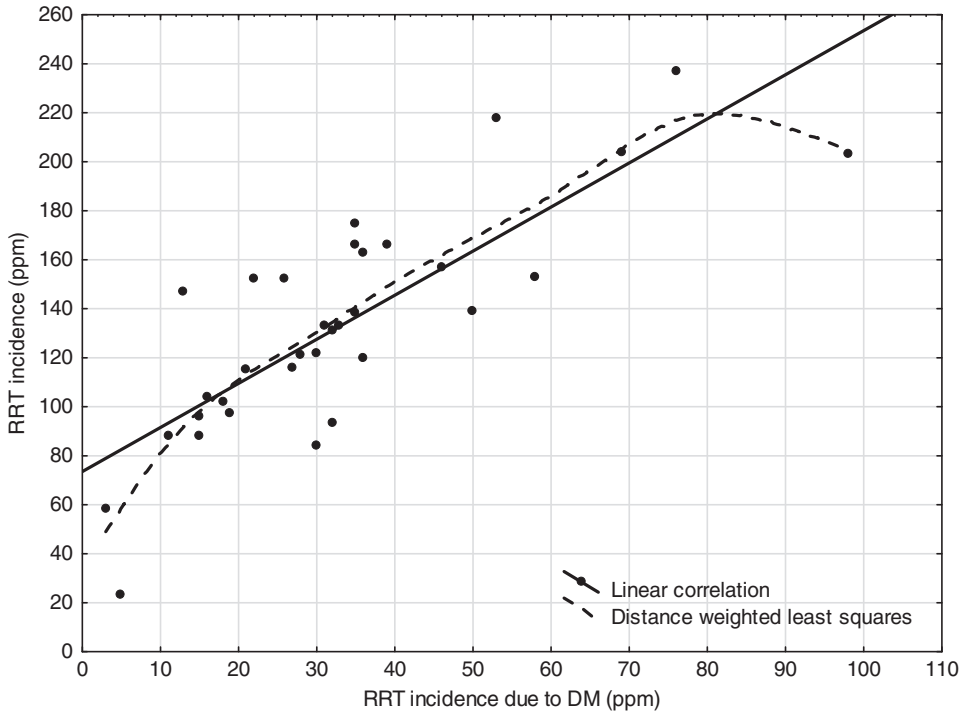

Fig. 2. Relationship of RRT incidence due to diabetes mellitus (DM) to overall unadjusted RRT in Europe in 2014. Incidence: unadjusted figures in patients/million population (ppm)/year. Linear correlation: $r = 0.81$, $P < 0.001$.

RRT incidence and GDP per capita in Europe (Fig. 1), some Eastern European countries with low GDP have low rates, suggesting that socioeconomic factors still play a part in RRT acceptance rates. Previous studies have shown that economic factors cease to be important once per capita GDP exceeds ~US$20 000/year [38]. RRT incidence for most of these countries is increasing and will probably continue to do so in the future. Other factors of importance in determining the wide variation in incidence are genetics [39, 40] birth weight [41], exercise [42], DM prevalence, dietary habits [43] and prophylactic measures, e.g., control of acidosis [44], hypertension (particularly by RAS blockade) [45] and reduction of obesity [46] and tobacco consumption [47, 48]. Middle income countries have generally high rates (Fig. 1), suggesting that while access to RRT for these countries is not limited by economic factors, prophylactic programs are not fully developed. The correlation between RRT due to diabetic nephropathy and overall RRT is virtually linear (Fig. 2): ~50% of the difference in RRT incidence rates is accounted for by differences in RRT due to diabetic nephropathy.

These observations suggest that the pattern of European RRT incidence in the future will be complex, with some countries demonstrating a low but increasing incidence, others a stable pattern and others a, hopefully expanding, group showing continuing reductions in adjusted incidence and eventually absolute incidence.

Relative modality prevalence

Several factors influence the relative modality prevalence. Initial modality choice, defined as the relative prevalence at 91 days after RRT initiation is an important factor. Preemptive transplantation, a highly desirable treatment, has increased from 3% in 2007 [11] to 5% in 2010 [2] to 6% now. Initial PD treatment has fallen from 15 to 13%, probably because many elderly patients are incapable of home treatment and because assisted PD in the home is not universally available. Second, transplantation activity will affect transplant prevalence. The number of transplantations has increased from 29 to 36 ppm since 2010 [2]. Third, since patient mortality on dialysis is about three times higher than with transplantation, the proportion of renal transplant patients will be expected to increase even in the absence of incidence changes. On the other hand, since the number of elderly patients, who are often unsuitable for transplantation, continues to increase, this will tend to reduce relative transplant prevalence. Since 2010, the relative prevalences of HD/PD/renal transplant has changed from 59/6/35 to 57/5/37%. An increase in the proportion of renal transplant patients will lead to improved overall RRT survival even in the absence of therapeutic improvements.

Conclusion

The importance of the ERA-EDTA Registry cannot be overemphasized. It is the world's largest international registry, contributing substantially to international comparisons. It forms the basis for much health resource planning. In cooperation with the European Society for Paediatric Nephrology, it is a valuable source of epidemiological research, generating some 90 publications during the last 10 years. Under the umbrella organization of the QUEST (Quality European STudies) initiative [17], international research programs have been initiated, including the EQUAL [49] and EVEREST [37, 50] studies. The registry's main handicap is incomplete data registration, in that only 17 of 35 countries are at present contributing detailed individual data. This is a natural consequence of its voluntary nature. It is hoped that an increasing recognition of the registry's value and improvements in local organization will improve this figure.

Acknowledgement

Many thanks to Maria Pippias for manuscript revision.

CLINICAL KIDNEY JOURNAL

Conflict of interest statement

None declared.

References

1. Pippias M. The European Renal Association-European Dialysis and Transplant Association (ERA-EDTA) Registry Annual Report 2014: a summary. *Clin Kidney J* 2017; 10: 1–10
2. Kramer A, Stel VS, Abad Diez JM *et al*. Renal replacement therapy in Europe—a summary of the 2010 ERA-EDTA Registry Annual Report. *Clin Kidney J* 2013; 6: 105–115
3. Noordzij M, Kramer A, Abad Diez JM *et al*. Renal replacement therapy in Europe: a summary of the 2011 ERA-EDTA Registry Annual Report. *Clin Kidney J* 2014; 7: 227–238
4. Pippias M, Stel VS, Abad Diez JM *et al*. Renal replacement therapy in Europe: a summary of the 2012 ERA-EDTA Registry Annual Report. *Clin Kidney J* 2015; 8: 248–261
5. Kramer A, Pippias M, Stel VS *et al*. Renal replacement therapy in Europe: a summary of the 2013 ERA-EDTA Registry Annual Report with a focus on diabetes mellitus. *Clin Kidney J* 2016; 9: 457–469
6. Stengel B, Billon S, van Dijk PC *et al*. Trends in the incidence of renal replacement therapy for end-stage renal disease in Europe, 1990–1999. *Nephrol Dial Transplant* 2003; 18: 1824–1833
7. van Dijk PC, Jager KJ, Stengel B *et al*. Renal replacement therapy for diabetic end-stage renal disease: data from 10 registries in Europe (1991–2000). *Kidney Int* 2005; 67: 1489–1499
8. Kramer A, Stel V, Zoccali C *et al*. An update on renal replacement therapy in Europe: ERA-EDTA Registry data from 1997 to 2006. *Nephrol Dial Transplant* 2009; 24: 3557–3566
9. Zoccali C, Kramer A, Jager K. The databases: renal replacement therapy since 1989—the European Renal Association and European Dialysis and Transplant Association (ERA-EDTA). *Clin J Am Soc Nephrol* 2009; 4(Suppl 1): S18–S22
10. Pippias M, Jager KJ, Kramer A *et al*. The changing trends and outcomes in renal replacement therapy: data from the ERA-EDTA Registry. *Nephrol Dial Transplant* 2016; 31: 831–841
11. van de Luijtgaarden MW, Jager KJ, Segelmark M *et al*. Trends in dialysis modality choice and related patient survival in the ERA-EDTA Registry over a 20-year period. *Nephrol Dial Transplant* 2016; 31: 120–128
12. Alberts C., Drukker W. Report on regular dialysis in Europe. *Proc Eur Dial Transplant Assoc* 1965; 2: 82–94
13. Brunner FP, Gurland HJ, Harlen H *et al*. Combined report on regular dialysis and transplantation in Europe, II, 1971. *Proc Eur Dial Transplant Assoc* 1972; 9: 3–34
14. van Dijk PC, Jager KJ, de CF *et al*. Renal replacement therapy in Europe: the results of a collaborative effort by the ERA-EDTA registry and six national or regional registries. *Nephrol Dial Transplant* 2001; 16: 1120–1129
15. Jager KJ, van Dijk PC. Has the rise in the incidence of renal replacement therapy in developed countries come to an end? *Nephrol Dial Transplant* 2007; 22: 678–680
16. Sorensen VR, Hansen PM, Heaf J *et al*. Stabilized incidence of diabetic patients referred for renal replacement therapy in Denmark. *Kidney Int* 2006; 70: 187–191
17. Jager KJ, Zoccali C. QUality European STudies (QUEST)—a step forward in the quality of RRT care. *Nephrol Dial Transplant* 2005; 20: 2005–2006
18. Heaf JG. Danish Nephrology Registry (DNR)—Annual Report 2015. http://www.nephrology.dk/Publikationer/Landsregister/%C3%85rsrapport%202015.pdf 2015; p. 34–35 (23 November 2016, date last accessed).
19. Heaf JG, Wehberg S. Reduced incidence of end stage renal disease among the elderly in Denmark: an observational study. *BMC Nephrol* 2012; 13: 131
20. United States Renal Data System. *2016 USRDS annual data report: Epidemiology of kidney disease in the United States*. National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, MD, 2016.
21. Global Report on Diabetes. World Health Organisation, 2016. http://apps.who.int/iris/bitstream/10665/204871/1/9789241565257_eng.pdf
22. Finne P, Grönhagen-Riska C. Finnish Registry for Kidney Diseases—Report 2014, p. 29. http://www.muma.fi/files/2154/Finnish_Registry_for_Kidney_Diseases_2014.pdf (23 November 2016, date last accessed)
23. Suki WN, Zabaneh R, Cangiano JL *et al*. Effects of sevelamer and calcium-based phosphate binders on mortality in hemodialysis patients. *Kidney Int* 2007; 72: 1130–1137
24. Wanner C, Krane V, Marz W *et al*. Atorvastatin in patients with type 2 diabetes mellitus undergoing hemodialysis. *N Engl J Med* 2005; 353: 238–248
25. Fellstrom BC, Jardine AG, Schmieder RE *et al*. Rosuvastatin and cardiovascular events in patients undergoing hemodialysis. *N Engl J Med* 2009; 360: 1395–1407
26. Chertow GM, Block GA, Correa-Rotter R *et al*. Effect of cinacalcet on cardiovascular disease in patients undergoing dialysis. *N Engl J Med* 2012; 367: 2482–2494
27. Kalantar-Zadeh K, Kuwae N, Regidor DL *et al*. Survival predictability of time-varying indicators of bone disease in maintenance hemodialysis patients. *Kidney Int* 2006; 70: 771–780
28. Teng M, Wolf M, Ofsthun MN *et al*. Activated injectable vitamin D and hemodialysis survival: a historical cohort study. *J Am Soc Nephrol* 2005; 16: 1115–1125
29. Georgianos PI, Agarwal R. Epidemiology, diagnosis and management of hypertension among patients on chronic dialysis. *Nat Rev Nephrol* 2016; 12: 636–647
30. Davies SJ. Mitigating peritoneal membrane characteristics in modern peritoneal dialysis therapy. *Kidney Int Suppl* 2006; 103: S76–S83
31. Smart NA, Dieberg G, Ladhani M *et al*. Early referral to specialist nephrology services for preventing the progression to end-stage kidney disease. *Cochrane Database Syst Rev* 2014; 6: CD007333
32. van de Luijtgaarden MW, Noordzij M, Stel VS *et al*. Effects of comorbid and demographic factors on dialysis modality choice and related patient survival in Europe. *Nephrol Dial Transplant* 2011; 26: 2940–2947
33. Heaf JG, Wehberg S. Relative survival of peritoneal dialysis and haemodialysis patients: effect of cohort and mode of dialysis initiation. *PLoS One* 2014; 9: e90119
34. Moist LM, Port FK, Orzol SM *et al*. Predictors of loss of residual renal function among new dialysis patients. *J Am Soc Nephrol* 2000; 11: 556–564
35. Foley RN, Gilbertson DT, Murray T, Collins AJ. Long interdialytic interval and mortality among patients receiving hemodialysis. *N Engl J Med* 2011; 365: 1099–1107
36. Burton JO, Jefferies HJ, Selby NM, McIntyre CW. Hemodialysis-induced cardiac injury: determinants and associated outcomes. *Clin J Am Soc Nephrol* 2009; 4: 914–920
37. Caskey FJ, Kramer A, Elliott RF *et al*. Global variation in renal replacement therapy for end-stage renal disease. *Nephrol Dial Transplant* 2011; 26: 2604–2610
38. White SL, Chadban SJ, Jan S *et al*. How can we achieve global equity in provision of renal replacement therapy? *Bull World Health Org* 2008; 86: 229–237

39. Kottgen A, Glazer NL, Dehghan A *et al*. Multiple loci associated with indices of renal function and chronic kidney disease. *Nat Genet* 2009; 41: 712–717
40. Boger CA, Gorski M, Li M *et al*. Association of eGFR-related loci identified by GWAS with incident CKD and ESRD. *PLoS Genet* 2011; 7: e1002292
41. Silverwood RJ, Pierce M, Hardy R *et al*. Low birth weight, later renal function, and the roles of adulthood blood pressure, diabetes, and obesity in a British birth cohort. *Kidney Int* 2013; 84: 1262–1270
42. Stengel B, Tarver-Carr ME, Powe NR *et al*. Lifestyle factors, obesity and the risk of chronic kidney disease. *Epidemiology* 2003; 14: 479–487
43. Chrysohoou C, Panagiotakos DB, Pitsavos C *et al*. Adherence to the Mediterranean diet is associated with renal function among healthy adults: the ATTICA study. *J Ren Nutr* 2010; 20: 176–184
44. de Brito-Ashurst I, Varagunam M, Raftery MJ, Yaqoob MM. Bicarbonate supplementation slows progression of CKD and improves nutritional status. *J Am Soc Nephrol* 2009; 20: 2075–2084
45. Jafar TH, Stark PC, Schmid CH *et al*. Progression of chronic kidney disease: the role of blood pressure control, proteinuria, and angiotensin-converting enzyme inhibition: a patient-level meta-analysis. *Ann Intern Med* 2003; 139: 244–252
46. Bonnet F, Deprele C, Sassolas A *et al*. Excessive body weight as a new independent risk factor for clinical and pathological progression in primary IgA nephritis. *Am J Kidney Dis* 2001; 37: 720–727
47. Orth SR, Stockmann A, Conradt C *et al*. Smoking as a risk factor for end-stage renal failure in men with primary renal disease. *Kidney Int* 1998; 54: 926–931
48. Pinto-Sietsma SJ, Mulder J, Janssen WM *et al*. Smoking is related to albuminuria and abnormal renal function in nondiabetic persons. *Ann Intern Med* 2000; 133: 585–591
49. Jager KJ, Ocak G, Drechsler C *et al*. The EQUAL study: a European study in chronic kidney disease stage 4 patients. *Nephrol Dial Transplant* 2012; 27(Suppl. 3): iii27–iii31
50. Caskey FJ, Jager KJ. A population approach to renal replacement therapy epidemiology: lessons from the EVEREST study. *Nephrol Dial Transplant* 2014; 29: 1494–1499